WS1.5 The use of bedside ultrasonography to identify delayed gastric emptying in cystic fibrosis

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Objectives: The gastric emptying rate (GER) may be delayed in CF, but its assessment is problematic and previous CF studies have employed scintigraphic techniques which are expensive and unsuitable for routine use. We wished to assess the use of ultrasonography for this purpose, which has been validated in a non-CF population using a 3.5-MHz abdominal transducer probe measuring gastric antral size [1].
Methods: After an overnight fast, in the supine position we looked at 12 non-diabetic subjects (mean age 26 [SD 4] years, 9 male) comparing the GER in 8 pancreatic insufficient CF patients with 4 healthy controls. Subjects consumed 113 mls (made up to 200 mls with water) of Polycal®, a liquid energy supplement. Ultrasound measurements were made regularly over 2 hours and gastric emptying >63% at 90 minutes was considered normal.
Results: There was a significant decrease in GER at 90 minutes ($p = 0.04$) and 120 minutes ($p = 0.02$) in the CF group (see table).
Conclusions: Delayed gastric emptying occurs in pancreatic insufficient patients with CF and without known cystic-fibrosis related diabetes. The novel use of bedside ultrasound in this patient group will allow timely management of patients with gastro-paresis by dietary manipulation or prokinetic therapy.

Gastric Emptying Rate (%) [Median (IQ range)]

Group	30 minutes	60 minutes	90 minutes	120 minutes
Control	39 (36–43)	49 (47–52)	68 (67–70)	75 (74–76)
CF	26 (18–40)	40 (37–47)	49 (47–63)	64 (62–72)
p value	0.16	0.23	0.04	0.02

Reference(s)

[1] Darwiche G et al. *J Ultrasound Med.* 1999;**18:**673–682.

WS1.6 The need of an appropriate diagnosis of gastroesophageal reflux disease in cystic fibrosis patients: impact on clinical management

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Objectives and Study: The use of proton pump inhibitors (PPI) is diffuse among Cystic Fibrosis (CF) patients to treat fat malabsorption and/or Gastro-esophageal Reflux Disease (GERD).
The aim of this prospective study was to assess an early diagnosis of GERD and the appropriate use of PPI in CF patients.
Methods: We enrolled CF patients aged 4 years and older, taking chronic PPI therapy or asymptomatic for typical GERD symptoms but showing a progressive lung deterioration.
All patients underwent pH-multichannel intraluminal impedance (pH-MII). GERD patients underwent upper endoscopy and gastric scintigraphy labelled with 99mTc-DTPA to study the esophageal transit and the gastric emptying.
Results: Since October 2010, 31 consecutive CF patients (female 19, mean age 20.1 yrs, range: 6–45) were enrolled. Eleven children did not take PPI therapy because they were symptom-free.
pH-MII detected GERD in 22/31 (71%) patients; all patients with severe GERD started PPI therapy, including 9/11 (82%) patients without typical GERD symptoms. PPI therapy was stopped in 5/31 patients (16.1%) with negative pH-MII and also in 3/31 patients (9.7%) with mild GERD and without symptoms. Gastric scintigraphy was performed in 17/22 (77%) GERD patients and showed a delayed esophageal transit and gastric emptying in 8/17 (47%) and 12/17 (70.6%) patients, respectively. Two patients (2/22) with severe esophagitis and pathologic scintigraphy underwent surgery.
Conclusion: GERD management was changed in more than 60% of patients. Our results underline the need of a correct diagnostic algorithm for GERD in CF patients to allow an appropriate treatment.

WS1.7 Gastroesophageal reflux in adult cystic fibrosis: a primary phenomenon or secondary to respiratory dysfunction?

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It has been suggested that gastroesophageal reflux (GER) in CF is a primary phenomenon, since reflux occurs already at young age. Reflux occurs mostly during transient lower esophageal sphincter relaxations (TLESR). We showed that reflux during TLESR is mostly due to an increased gastroesophageal pressure gradient (GEPG), caused by decreased intra-thoracic pressures (ITP).
We **aimed** to assess the relation between magnitude of respiratory oscillations and GER in CF.
Methods: 12 CF adults and 11 age and sex-matched healthy subjects were studied using high resolution manometry-impedance. In the thorax, expiration provokes slightly positive pressure that becomes negative in inspiration, which is opposite in the abdomen. GEPG was calculated by subtracting ITP from intra-abdominal pressure (IAP).
Results: GEPG in expiration was similar in CF and healthy. However, GEPG was significantly higher in CF patients compared to healthy subjects during inspiration [13.1 (9.9–15.8) vs. 7.1 (4.5–9.4) mmHg, $p = 0.005$]. This was due to significantly lower ITP in CF [−7.5 (−10.6 – (−5.6)) vs. 0.07 (−6–1.1) mmHg, $p = 0.003$]. In CF, 77 (67–85)% of the reflux episodes started during inspiration vs. 23 (15–33)% in expiration ($p < 0.0001$). In healthy subjects, reflux occurred in both respiratory phases.
Conclusion: CF patients have reflux during TLESR due to high GEPG which was caused by decreased thoracic pressures. This is particularly significant during the inspiratory phase of respiratory oscillations. Most TLESR-related reflux in CF starts in inspiration. The increased inspiratory effort in CF can favor reflux suggesting that in CF adults reflux can be a secondary phenomenon to respiratory dysfunction.

WS1.8 Risks of PPI treatment in patients with cystic fibrosis: effect of gastric juice of patients "on" PPI on IL-8 production by CF primary bronchial epithelial cells

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Patients with CF are often treated with proton pump inhibitors (PPI) to reduce acidic gastroesophageal reflux (GER). Duodeno-gastric aspiration is common in CF. We showed that gastric juice (GJ) from patients "on" PPI can induce high IL-8 levels by bronchial epithelial cells, mainly related to increased bacterial sub-products.
We **aimed** to evaluate the effect of GJ "on" PPI on IL-8 production by CF primary bronchial epithelial cells (CF-PBEC) and compare this with healthy PBEC (H-PBEC).
Methods: PBEC, obtained at lung transplantation were stimulated with GJ "off" PPI (1/1000) and GJ "on" PPI (1/1000). IL-8 levels were measured in supernatant.
Results: GJ "off" PPI provoked lower IL-8 production than GJ "on" PPI, both in H-PBEC [11.4 (4.2–28.1) vs. 462.9 (200.3–1468) pg/ml, $p = 0.0001$] as in CF-PBEC [85.2 (25.6–131.2) vs. 1468 (841.4–2449) pg/ml, $p < 0.0001$]. Exposure of cells to GJ "off" PPI and "on" PPI provoked higher IL-8 production in CF-PBEC compared to H-PBEC ["off" 85.2 (25.6–131.2) vs. 11.4 (4.2–28.1) pg/ml, $p = 0.02$; "on" 1468 (841.4–2449) vs. 462.9 (200.3–1468) pg/ml, $p = 0.04$]. Filtration of the GJ "on" PPI reduced IL-8 production, both in H-PBEC as in CF-PBEC. There was a correlation between IL-8 and the pH of GJ, both in H-PBEC ($r = 0.66$) as in CF-PBEC ($r = 0.73$).
Conclusion: CF patients, treated with PPI, have non-acidic GJ and bacterial contamination and often do aspirate. The aspirated material has an enhanced inflammatory effect on CF-PBEC. Our data suggest that chronic PPI treatment in CF may result in a paradoxically increased inflammatory effect in the airways. Alternative anti-reflux therapies should be considered in CF with increased GER and demonstrated aspiration.